

REMARKS

Upon entry of the present amendment, claims 1-19 are pending in the above-referenced patent application and are currently under examination. Claims 1 and 12 have been amended. Claims 20-22 have been canceled. Claims 5-7 have been withdrawn. Reconsideration of the application is respectfully requested.

Claim 1 has been amended to more clearly define the invention of the instant application by providing in the body of the claim that administration of the glucocorticoid receptor antagonist is to a "patient having received interferon α therapy and suffering from psychosis associated with the interferon α therapy." Support for this amendment can be found throughout the specification, particularly in paragraph [05] and Example 1.

Claim 12 has been amended to correct a spelling error. Applicants thank the Examiner for noting the spelling error.

Applicants believe the claim amendments add no new matter to the claims.

Applicants thank the Examiner for the telephone call of April 25, 2007 to Ken Weber and for the opportunity to make a provisional election. Applicants confirm the election of the glucocorticoid receptor antagonist mifepristone of claim 4.

The claims are rejected in various combinations under 35 U.S.C. §§ 102(a), (b), (e) and 103(a). In addition, claims 8 and 12 have been objected to. Each of these rejections and objections is addressed below in the order set forth by the Examiner.

I. OBJECTIONS

Claim 8 has been objected to as allegedly lacking a period at the end of the claim. Applicants respectfully note that such period is in fact present, and is simply sufficiently close to the " α " that it appears to be part of the " α ." Accordingly, no amendment has been made.

Claim 12 has also been objected to as containing a spelling error. Applicants note that claim 12 has been amended to correct the spelling error.

II. REJECTION UNDER 35 U.S.C. § 102(b) OVER SCHATZBERG

Claims 1-4 and 13-19 have been rejected under 35 USC § 102(b) as allegedly being anticipated in view of Schatzberg. Applicants respectfully traverse the rejections in view of the comments below.

A claim is considered to be anticipated under 35 USC § 102(b) if “the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.” In order for a claim to be anticipated by a reference, the reference must teach every element of the claim (MPEP § 2131, citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). As discussed in detail below, the presently claimed invention is not anticipated in view of any of the cited references as all the references fail to teach every element set forth in the claims of the instant invention.

The Examiner alleges that the claims of the instant application are anticipated by Schatzberg. Applicants respectfully traverse the rejection in view of the comments below.

The instantly amended claims are drawn to treatment of a patient population that is suffering from interferon- α induced psychosis and that receives treatment with a glucocorticoid receptor antagonist (GRA) to ameliorate the psychosis, such that the patient is not otherwise in need of treatment with a GRA. Accordingly, the patient population receives GRA treatment only after presenting with interferon- α induced psychosis.

The psychosis resulting from interferon- α therapy is a *symptom*, not a disease. Schatzberg discloses psychosis stemming from psychotic major depression. Other conditions such as fever, schizophrenia, schizo-effective disorder and treatment with interferon- α , also lead to the *symptom* of psychosis. While these different diseases all lead to the symptom of psychosis, the resultant symptom of psychosis requires different treatments in order to ameliorate. Not all psychoses are treatable with a GRA.

The instantly amended claims recite a “patient having received interferon α therapy and suffering from psychosis associated with the interferon α therapy.” In contrast, Schatzberg discloses a method of ameliorating psychosis associated with **psychotic major**

depression by administering an effective amount of a GRA, such as mifepristone. There is absolutely no disclosure in Schatzberg regarding treatment of a patient with interferon- α therapy, where that patient suffers from psychosis associated with the interferon- α therapy. As Schatzberg fails to teach all the elements of the instantly amended claims, the instantly amended claims are not anticipated under 35 U.S.C. § 102(b) over Schatzberg. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

III. REJECTION UNDER 35 U.S.C. § 102(a)/102(e) OVER RUBINFELD

Claims 20-22 have been rejected under 35 USC § 102(a)/102(e) as allegedly being anticipated in view of Rubinfeld. Applicants respectfully traverse the rejections in view of the comments below.

Applicants respectfully note that claims 20-22 have been cancelled. Accordingly, Applicants respectfully note that this aspect of the rejection is now moot.

IV. REJECTION UNDER 35 U.S.C. § 103(a) OVER KORANT & BOZIKAS

Claims 1-4, 8-12 and 16-17 have been rejected under 35 USC § 103(a) as allegedly being obvious over Korant in view of Bozikas. Applicants respectfully traverse the rejection in view of the comments below.

The Examiner alleges it would have been obvious to ameliorate the symptoms of psychosis associated with interferon- α therapy comprising administering a glucocorticoid receptor antagonist (GRA), interferon- α and ribavirin. Applicants respectfully disagree.

Korant discloses treatment of a patient population suffering from a chronic viral infection where the patients are treated with a cytotoxic agent that might have GRA activity and an antiviral agent (interferon- α). Bozikas discloses a patient population suffering from interferon- α induced psychosis, but not treatment of the interferon- α induced psychosis with a GRA.

A claim is considered obvious “if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains” (35 USC § 103(a)). In order for the claims of the instant

application to be obvious in view of the cited art, the prior art reference (or combination of references) must (1) teach or suggest the claim elements; (2) provide some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; and (3) provide a reasonable expectation of success of making the claimed invention (MPEP § 2143). As discussed in detail below, none of the cited references satisfies all three requirements under MPEP § 2143.

A. There is No Suggestion or Motivation to Combine Korant and Bozikas

The Examiner asserts that one of skill in the art would have been motivated to treat interferon- α induced psychosis with the combination of a GRA, interferon- α and ribavirin because Korant suggests the combination of a GRA (**cytotoxic agent** cyproterone acetate) with interferon- α and ribavirin. The Examiner also asserts that it would be obvious to ameliorate interferon- α induced psychosis as claimed in the instant application because “the method of Bozikas is composed of the same ingredients” (page 10 of Office Action, bottom of 2d paragraph). Applicants respectfully disagree.

The combination of Korant and Bozikas fails to suggest or motivate those of skill in the art to use a GRA to treat interferon- α induced psychosis.

The patient population of Korant suffers from a chronic viral infection that is treated with a **cytotoxic agent** and an antiviral agent (interferon- α). The Examiner points to a single **cytotoxic agent** (cyproterone acetate, col. 4, line 5) as having GRA activity. While the cyproterone acetate the Examiner relies upon may have some GRA activity, Korant teaches the use of the cyproterone acetate as a **cytotoxic agent**, an agent used to kill cells. Korant discloses the cyproterone acetate as useful only as a **cytotoxic agent**. There is no teaching in Korant that the GRA activity of the cyproterone acetate is medically significant at doses useful to treat interferon- α induced psychosis or that minimize the cytotoxic effect of the cyproterone acetate. Thus, one of skill in the art, provided with the disclosure in Korant of the combination of the **cytotoxic agent** cyproterone acetate and interferon- α , would not be motivated to treat interferon- α induced psychosis with a GRA.

Bozikas discloses the onset of psychotic symptoms following treatment with interferon- α for a hepatitis C infection, and treatment with anti-psychotics that are not GRAs.

The Examiner is apparently relying on Korant to provide the missing element from Bozikas of treatment of interferon- α induced psychosis with a GRA. As discussed above, Korant discloses treatment of chronic viral infections with the **cytotoxic agent** cyproterone acetate. It is the alleged GRA activity of the cyproterone acetate which the Examiner relies on to assert that Korant and Bozikas can be combined. While the cyproterone acetate has some GRA activity, even general encyclopedias describe cyproterone acetate as having “weak ... glucocorticoid activity” (see Wikipedia at http://en.wikipedia.org/wiki/Cyproterone_acetate). Since there is no teaching in Korant that the GRA activity of the **cytotoxic agent** cyproterone acetate is effective at doses useful to treat interferon- α induced psychosis with minimal cytotoxic effect, Applicants respectfully submit that Korant fails to provide the necessary suggestion or motivation to combine with Bozikas.

In addition to lacking the necessary motivation, Applicants would again like to point out that interferon- α induced psychosis is a *symptom*, not a disease. As discussed above, Schatzberg discloses psychosis stemming from psychotic major depression. Other conditions such as fever, schizophrenia, schizo-effective disorder and treatment with interferon- α , also lead to the *symptom* of psychosis. But not all psychoses are treatable with GRAs. For example, Applicants have tested mifepristone in patients with schizo-effective disorder and schizophrenia. The GRA treatment did not ameliorate the psychosis. Accordingly, one of skill in the art knowing of treatment of psychosis and having read Korant and Bozikas, would not appreciate that interferon- α induced psychosis is treatable with a GRA. As the patient population of Korant is limited to treatment of chronic viral infections, Korant by itself does not provide the necessary suggestion or motivation to modify the reference or combine with Bozikas.

Having explained that psychosis is a symptom of many different diseases and is treated in a variety of ways, Applicants would like to further explain why there could be no motivation using a hypothetical example. For Korant to be a material reference against the instant claims, a patient suffering from hepatitis-C and being treated with interferon- α but not suffering from psychosis, would have to present themselves to a physician who would then elect

to keep the patient on interferon- α and then treat with a cytotoxic agent that may or may not have ancillary GRA activity. But is this realistic?

For references to be at least sufficient for a *prima facie* combination, one has to go beyond blind luck to make the combination. In the instant invention, the compound administered to ameliorate the interferon- α induced psychosis has glucocorticoid activity that is *effective* to treat the psychosis, as opposed to having some glucocorticoid activity.

In view of the absence of the necessary teachings, Korant and Bozikas fail to provide the necessary suggestion or motivation to modify either reference or to combine, as required for a *prima facie* case of obviousness under 35 U.S.C. § 103(a). Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

B. There is no Expectation of Success

Even if there was motivation to combine Korant and Bozikas, there is no expectation of success provided by the combination of making the claimed invention.

As noted above, Korant discloses a patient population suffering from a chronic viral infection and treatment with a cytotoxic agent and an antiviral agent (interferon- α). In addition, there is no disclosure in Korant that the **cytotoxic agent** cyproterone acetate relied upon has any medically significant GRA activity at doses useful to treat interferon- α induced psychosis with minimal cytotoxic effect. Thus, in order to teach the present invention of treatment with a GRA to ameliorate interferon- α induced psychosis, the Examiner is relying upon a reference disclosing a cytotoxic agent with ancillary GRA activity and a reference disclosing identification of psychosis following interferon- α treatment in a patient with chronic hepatitis C. Applicants respectfully submit that the combination of Korant and Bozikas fails to provide the necessary expectation of success of making the claimed invention. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

As neither Korant nor Bozikas provide the necessary motivation to modify or combine the references nor the requisite expectation of success, the combination of Korant and Bozikas fails to meet all the elements for a *prima facie* case of obviousness under 35 U.S.C. §

Appl. No. 10/519,008
Amdt. dated October 3, 2007
Reply to Office Action of May 4, 2007

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103(a). Thus, the instantly amended claims are not obvious. Accordingly, Applicants respectfully request that the Examiner withdraw this aspect of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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